

WHAT IS CLAIMED IS:

1. A method of treating a neurological disorder associated with synaptic vesicle function, endocrinopathy or hormonal diseases, comprising administering a compound or agent that modulates a function or activity of an SV2 protein.
5
2. A method of claim 1, wherein the neurological disorder is a seizure disorder.
3. A method of claim 1, wherein the neurological disorder is selected from the group consisting of epilepsy, Parkinson's disease, Parkinson's dyskinesias, migraine, Alzheimer's disease, neuropathic pain, essential tremor, cognitive disorders, and movement disorders.
10
4. A method of claim 1, wherein the compound or agent binds to the levetiracetam binding site of an SV2 protein.
15
5. A method of claim 4, wherein the compound or agent is levetiracetam or an analog or derivative thereof.
6. A method of claim 5, wherein the analog or derivative of levetiracetam is (2S)-2-[4-(3-azidophenyl)-2-oxopyrrolidin-1-yl]butanamide.
20
7. A method of claim 5, wherein the analog or derivative of levetiracetam is selected from the group consisting of N-alkylated 2-oxo-pyrrolidine derivatives, N-alkylated 2-oxo-piperidinyll derivatives, and N-alkylated 2-oxo-azepanyl derivatives.
25
8. A method of claim 4, wherein the compound or agent competes with levetiracetam or an analog or derivative thereof for binding to the levetiracetam binding site.
9. A method of claim 1, wherein the compound or agent is an anti-SV2 antibody or fragment thereof.
30

10. A method of claim 9, wherein the anti-SV2 antibody or fragment thereof binds to the levetiracetam binding site of SV2 protein.

11. A method of claim 9, wherein the anti-SV2 antibody or fragment thereof is selected
5 from the group consisting of a polyclonal antibody and a monoclonal antibody.

12. A method of claim 11, wherein the antibody fragment is selected from the group consisting of an Fab fragment, Fab' fragment, F(ab')₂ fragment and an scFv fragment.

10 13. A method of claim 11, wherein the monoclonal antibody is selected from the group consisting of a chimeric antibody, a humanized antibody, and a human antibody.

14. A method of claim 1, wherein the SV2 protein is SV2A.

15 15. A method of modulating at least one function or activity of a SV2 protein in a cell, comprising exposing the cell to a compound or agent that binds to the levetiracetam binding site of the SV2 protein.

16. A method of claim 15, wherein the compound or agent is levetiracetam or an analog
20 or derivative thereof.

17. A method of claim 16, wherein the analog or derivative of levetiracetam is (2S)-2-[4-(3-azidophenyl)-2-oxopyrrolidin-1-yl]butanamide.

25 18. A method of claim 16, wherein the analog or derivative of levetiracetam is selected from the group consisting of N-alkylated 2-oxo-pyrrolidine derivatives, N-alkylated 2-oxo-piperidinyll derivatives, and N-alkylated 2-oxo-azepanyl derivatives.

19. A method of claim 15, wherein the compound or agent competes with levetiracetam
30 or an analog or derivative thereof for binding to the levetiracetam binding site.

20. A method of claim 19, wherein the compound or agent is an anti-SV2 antibody or fragment thereof.

21. A method of claim 20, wherein the anti-SV2 antibody or fragment thereof binds to the
5 levetiracetam binding site of SV2 protein.

22. A method of claim 20, wherein the anti-SV2 antibody or fragment thereof is selected from the group consisting of a polyclonal antibody and a monoclonal antibody.

10 23. A method of claim 22, wherein the antibody fragment is selected from the group consisting of an Fab fragment, Fab' fragment, F(ab')₂ fragment and an scFv fragment.

24. A method of claim 21, wherein the monoclonal antibody is selected from the group consisting of a chimeric antibody, a humanized antibody, and a human antibody.

15 25. A method of claim 15, wherein the compound or agent modulates the binding of levetiracetam to the levetiracetam binding site.

20 26. A method of claim 25, wherein the compound or agent is an analog or derivative of levetiracetam.

27. A method of claim 26, wherein the analog or derivative of levetiracetam is (2S)-2-[4-(3-azidophenyl)-2-oxopyrrolidin-1-yl]butanamide.

25 28. A method of claim 26, wherein the analog or derivative of levetiracetam is selected from the group consisting of N-alkylated 2-oxo-pyrrolidine derivatives, N-alkylated 2-oxo-piperidinyll derivatives, and N-alkylated 2-oxo-azepanyl derivatives.

29. A method of claim 25, wherein the compound or agent competes with levetiracetam
30 or an analog or derivative thereof for binding to the levetiracetam binding site.

30. A method of claim 25, wherein the compound or agent is an anti-SV2 antibody or fragment thereof.

31. A method of claim 30, wherein the anti-SV2 antibody or fragment thereof binds to the
5 levetiracetam binding site of SV2 protein.

32. A method of claim 30, wherein the anti-SV2 antibody or fragment thereof is selected from the group consisting of a polyclonal antibody and a monoclonal antibody.

10 33. A method of claim 32, wherein the antibody fragment is selected from the group consisting of an Fab fragment, Fab' fragment, F(ab')₂ fragment and an scFv fragment.

34. A method of claim 32, wherein the monoclonal antibody is selected from the group consisting of a chimeric antibody, a humanized antibody, and a human antibody.

15 35. A method of claim 15, wherein the SV2 protein is SV2A.

36. A method of discovering or modeling an interaction between an SV2 protein and a compound or agent selected from the group consisting of: levetiracetam, an analog or
20 derivative of levetiracetam, or a compound or agent which competes with levetiracetam or an analog or derivative thereof for binding to the levetiracetam binding site comprising:

- a) contacting the SV2 protein with the compound or agent; and
- b) measuring and analyzing the interaction of the SV2 protein with the compound or agent.

25 37. A method of claim 36, wherein the analysis is by 3-dimensional modeling or other purely computational techniques.

38. A method of claim 37, wherein the 3-dimensional modeling is via nuclear magnetic
30 resonance spectroscopy.

39. A method of claim 37, wherein the 3-dimensional modeling is via X-ray crystallography.

40. A method of claim 36, wherein the analysis is by binding studies.

5

41. A method of claim 36, wherein the compound or agent is labeled levetiracetam or a labeled analog or derivative thereof.

10

42. A method of claim 41, wherein the labeled analog or derivative of levetiracetam comprises (2S)-2-[4-(3-azidophenyl)-2-oxopyrrolidin-1-yl]butanamide.

15

43. A method of claim 41, wherein the labeled analog or derivative of levetiracetam is selected from the group consisting of N-alkylated 2-oxo-pyrrolidine derivatives, N-alkylated 2-oxo-piperidiny l derivatives, and N-alkylated 2-oxo-azepanyl derivatives.

20

44. A method of claim 36, wherein the compound or agent which competes with levetiracetam or an analog or derivative thereof for binding to the levetiracetam binding site is an anti-SV2 antibody or fragment thereof.

45. A method of claim 44, wherein the anti-SV2 antibody or fragment thereof binds to the levetiracetam binding site of SV2 protein.

25

46. A method of claim 44, wherein the anti-SV2 antibody or fragment thereof is selected from the group consisting of a polyclonal antibody and a monoclonal antibody.

47. A method of claim 46, wherein the antibody fragment is selected from the group consisting of an Fab fragment, Fab' fragment, F(ab')₂ fragment and an scFv fragment.

30

48. A method of claim 46, wherein the monoclonal antibody is selected from the group consisting of a chimeric antibody, a humanized antibody, and a human antibody.

49. A method of claim 36, wherein the SV2 protein is SV2A.

50. A method of identifying a levetiracetam binding site within an SV2 protein comprising;

5 a) contacting a SV2 protein or fragment thereof with a compound or agent selected from the group consisting of levetiracetam, an analog or derivative of levetiracetam, or a compound or agent which competes with levetiracetam or an analog or derivative thereof for binding to the levetiracetam binding site; and

10 b) determining the binding of the compound or agent with the SV2 protein or fragment thereof.

51. A method of claim 50, wherein the SV2 protein or fragment thereof comprises at least one amino acid substitution, deletion or addition.

15 52. A method of claim 51, wherein the addition, deletion or substitution of amino acid residues removes at least one glycosylation sites.

20 53. A method of claim 52, wherein the removal of glycosylation sites is *via* site-directed mutagenesis.

54. A method of claim 50, wherein the analog or derivative of levetiracetam is (2S)-2-[4-(3-azidophenyl)-2-oxopyrrolidin-1-yl]butanamide.

25 55. A method of claim 50, wherein the analog or derivative of levetiracetam is selected from the group consisting of N-alkylated 2-oxo-pyrrolidine derivatives, N-alkylated 2-oxo-piperidinyll derivatives, and N-alkylated 2-oxo-azepanyl derivatives.

30 56. A method of claim 50, wherein the compound or agent competes with levetiracetam or an analog or derivative thereof for binding to the levetiracetam binding site.

57. A method of claim 56, wherein the compound or agent is an anti-SV2 antibody or fragment thereof.

58. A method of claim 57, wherein the anti-SV2 antibody or fragment thereof binds to the
5 levetiracetam binding site of SV2 protein.

59. A method of claim 57, wherein the anti-SV2 antibody or fragment thereof is selected from the group consisting of a polyclonal antibody and a monoclonal antibody.

10 60. A method of claim 59, wherein the antibody fragment is selected from the group consisting of an Fab fragment, Fab' fragment, F(ab')₂ fragment and an scFv fragment.

61. A method of claim 59, wherein the monoclonal antibody is selected from the group consisting of a chimeric antibody, a humanized antibody, and a human antibody.

15 62. A method of claim 50, wherein the SV2 protein or fragment thereof is SV2A or a fragment thereof.

63. A method of claim 50, wherein the SV2 protein is a fusion protein comprising at least
20 one SV2 protein or fragment thereof and a fusion partner.

64. A method of claim 63, wherein the fusion partner is a fusion tag.

65. A method of claim 64, is a poly-His tag or glutathione-S-transferase.

25 66. A method of claim 63, wherein the fusion partner is attached to the N-terminus of the SV2 protein.

67. A method of claim 63, wherein the fusion partner is attached to the C-terminus of the
30 SV2 protein.

68. A method of assaying the interaction between SV2 protein and a second protein comprising;

- a) expressing SV2 protein and the protein of interest in a cell;
- b) exposing the cell to a compound or agent which binds to the levetiracetam binding site; and
- c) determining the interaction between the SV2 protein and the protein of interest.

69 A method of claim 68, wherein the second protein is selected from the group consisting of: a cell membrane protein, a vesicle membrane protein, a cytoplasmic protein, a cytoskeletal protein, and an intracellular matrix protein.

70. A method of claim 68, wherein the compound or agent is levetiracetam or an analog or derivative thereof.

71. A method of claim 70, wherein the analog or derivative of levetiracetam is (2S)-2-[4-(3-azidophenyl)-2-oxopyrrolidin-1-yl]butanamide.

72. A method of claim 70, wherein the analog or derivative of levetiracetam is selected from the group consisting of N-alkylated 2-oxo-pyrrolidine derivatives, N-alkylated 2-oxo-piperidinyl derivatives, and N-alkylated 2-oxo-azepanyl derivatives.

73. A method of claim 68, wherein the compound or agent competes with levetiracetam or an analog or derivative thereof for binding to the levetiracetam binding site.

74. A method of claim 73, wherein the compound or agent is an anti-SV2 antibody or fragment thereof.

75. A method of claim 74, wherein the anti-SV2 antibody or fragment thereof binds to the levetiracetam binding site of SV2 protein.

76. A method of claim 74, wherein the anti-SV2 antibody or fragment thereof is selected from the group consisting of a polyclonal antibody and a monoclonal antibody.

77. A method of claim 76, wherein the antibody fragment is selected from the group consisting of an Fab fragment, Fab' fragment, F(ab')₂ fragment and an scFv fragment.

78. A method of claim 76, wherein the monoclonal antibody is selected from the group consisting of a chimeric antibody, a humanized antibody, and a human antibody.

79. A method of claim 68, wherein the SV2 protein is SV2A.

80. A method of claim 68, wherein the protein of interest is synaptotagmin.

81. A method of claim 68, wherein the protein of interest is a member of the SNARE complex.

82. A method of claim 81, wherein the member of the SNARE complex is synaptic vesicle associated VAMP/synaptobrevin.

83. A method of claim 81, wherein the member of the SNARE complex is syntaxin.

84. A method of claim 81, wherein the member of the SNARE complex is SNAP-25.

85. A method of claim 68, wherein the step of exposing the cell to a compound or agent which binds to the levetiracetam binding site is carried out under conditions with a divalent cation concentration of less than about 1 μ M.

86. A method of claim 85, wherein the divalent cation is selected from the group consisting of Ca²⁺, Zn²⁺, Pb²⁺, Mg²⁺, Mn²⁺, Fe²⁺ and Cu²⁺.

87. A method of claim 68, wherein the step of exposing the cell to a compound or agent

which binds to the levetiracetam binding site is carried out under conditions with a divalent cation concentration of between about 1 μM and about 1000 μM .

88. A method of claim 87, wherein the divalent cation is selected from the group
5 consisting of Ca^{2+} , Zn^{2+} , Pb^{2+} , Mg^{2+} , Mn^{2+} , Fe^{2+} and Cu^{2+} .

89. A method of claim 68, wherein the step of exposing the cell to a compound or agent
which binds to the levetiracetam binding site is carried out under conditions with a divalent
cation concentration of at least about 1000 μM .

10 90. A method of claim 89, wherein the divalent cation is selected from the group
consisting of Ca^{2+} , Zn^{2+} , Pb^{2+} , Mg^{2+} , Mn^{2+} , Fe^{2+} and Cu^{2+} .

91. A method of claim 68, wherein the SV2 protein lacks at least one glycosylation site.

15 92. A method of claim 91, wherein the lack of at least one glycosylation site is due to site-
directed mutagenesis.

93. A method of identifying a compound or agent that modulates a neurological disorder
20 associated with synaptic function, endocrinopathy or hormonal disease comprising;

- a) exposing a SV2 protein to the compound or agent; and
- b) determining whether the compound or agent modulates an activity of the SV2
protein.

25 94. A method of claim 93, wherein the compound or agent is an analog or derivative of
levetiracetam.

95. A method of claim 94, wherein the analog or derivative of levetiracetam is selected
from the group consisting of N-alkylated 2-oxo-pyrrolidine derivatives, N-alkylated 2-oxo-
30 piperidinyll derivatives, and N-alkylated 2-oxo-azepanyl derivatives.

96. A method of claim 93, wherein the compound or agent competes with levetiracetam or an analog or derivative thereof for binding to the levetiracetam binding site.

97. A method of claim 96, wherein the compound or agent is an anti-SV2 antibody or
5 fragment thereof.

98. A method of claim 97, wherein the anti-SV2 antibody or fragment thereof binds to the levetiracetam binding site of SV2 protein.

99. A method of claim 97, wherein the anti-SV2 antibody or fragment thereof is selected
10 from the group consisting of a polyclonal antibody and a monoclonal antibody.

100. A method of claim 99, wherein the antibody fragment is selected from the group
consisting of an Fab fragment, Fab' fragment, F(ab')₂ fragment and an scFv fragment.

101. A method of claim 99, wherein the monoclonal antibody is selected from the group
consisting of a chimeric antibody, a humanized antibody, and a human antibody.

102. A method of claim 93, wherein the SV2 protein is SV2A.

103. A method of identifying a cellular response to a compound or agent selected from the
group consisting of levetiracetam, an analog or derivative of levetiracetam, or a compound or
agent which competes with levetiracetam or an analog or derivative thereof for binding to the
levetiracetam binding site comprising:

- 25 a) exposing cells expressing an SV2 protein to the compound or agent; and
 b) analyzing a change in the expression of a nucleic acid or protein in the
 exposed cell.

104. A method of claim 103, wherein the nucleic acid is RNA.

105. A method of claim 104, wherein RNA expression is analyzed by hybridization.

106. A method of claim 105, wherein the hybridization is on a microarray.

107. A method of claim 103, wherein the compound or agent is levetiracetam or an analog
5 or derivative thereof.

108. A method of claim 107, wherein the analog or derivative of levetiracetam is (2S)-2-[4-(3-azidophenyl)-2-oxopyrrolidin-1-yl]butanamide.

109. A method of claim 107, wherein the analog or derivative of levetiracetam is selected
10 from the group consisting of N-alkylated 2-oxo-pyrrolidine derivatives, N-alkylated 2-oxo-piperidinyll derivatives, and N-alkylated 2-oxo-azepanyl derivatives.

110. A method of claim 103, wherein the compound or agent competes with levetiracetam
15 or an analog or derivative thereof for binding to the levetiracetam binding site.

111. A method of claim 110, wherein the compound or agent is an anti-SV2 antibody or fragment thereof.

112. A method of claim 111, wherein the anti-SV2 antibody or fragment thereof binds to
20 the levetiracetam binding site of SV2 protein.

113. A method of claim 111, wherein the anti-SV2 antibody or fragment thereof is selected
25 from the group consisting of a polyclonal antibody and a monoclonal antibody.

114. A method of claim 113, wherein the antibody fragment is selected from the group
consisting of an Fab fragment, Fab' fragment, F(ab')₂ fragment and an scFv fragment.

115. A method of claim 113, wherein the monoclonal antibody is selected from the group
30 consisting of a chimeric antibody, a humanized antibody, and a human antibody.

116. A method of claim 103, wherein the SV2 protein is SV2A.

117. A method of claim 103, wherein the step of exposing the cell to a compound or agent which binds to the levetiracetam binding site is carried out under conditions with a divalent
5 cation concentration of less than about 1 μM .

118. A method of claim 117, wherein the divalent cation is selected from the group consisting of Ca^{2+} , Zn^{2+} , Pb^{2+} , Mg^{2+} , Mn^{2+} , Fe^{2+} and Cu^{2+} .

10 119. A method of claim 103, wherein the step of exposing the cell to a compound or agent which binds to the levetiracetam binding site is carried out under conditions with a divalent cation concentration of between about 1 μM and about 1000 μM .

120. A method of claim 119, wherein the divalent cation is selected from the group
15 consisting of Ca^{2+} , Zn^{2+} , Pb^{2+} , Mg^{2+} , Mn^{2+} , Fe^{2+} and Cu^{2+} .

121. A method of claim 103, wherein the step of exposing the cell to a compound or agent which binds to the levetiracetam binding site is carried out under conditions with a divalent cation concentration of at least about 1000 μM .

20 122. A method of claim 121, wherein the divalent cation is selected from the group consisting of Ca^{2+} , Zn^{2+} , Pb^{2+} , Mg^{2+} , Mn^{2+} , Fe^{2+} and Cu^{2+} .

123. An isolated nucleic acid molecule comprising the nucleic acid sequence of SEQ ID
25 NO: 5 or the complement thereof.

124. An isolated polypeptide comprising an amino acid sequence encoded by the isolated nucleic acid molecule of claim 123.

30 125. An isolated polypeptide of claim 124, comprising the amino acid sequence of SEQ ID NO: 6.

126. A method of claim 93, wherein the step of determining whether the compound or agent modulates an activity of the SV2 protein comprises measuring transport of at least one monovalent cation or divalent cation across a membrane.

5 127. A method of claim 126, wherein the monovalent cation is selected from the group consisting of H^+ , Cl^- , Na^+ and K^+ .

128. A method of claim 126, wherein the divalent cation is selected from the group consisting of Ca^{2+} , Zn^{2+} , Pb^{2+} , Mg^{2+} , Mn^{2+} , Fe^{2+} and Cu^{2+} .

10

129. A method of claim 128, wherein the at least one divalent cation is Ca^{2+} .

130. A method of claim 93, wherein the step of determining whether the compound or agent modulates an activity of the SV2 protein comprises measuring SNARE complex
15 formation.

131. A method of claim 93, wherein the step of determining whether the compound or agent modulates an activity of the SV2 protein comprises measuring Ca^{2+} channel formation or activity.

20

132. A method of claim 93, wherein the step of determining whether the compound or agent modulates an activity of the SV2 protein comprises measuring SV2 interaction with at least one other protein.

25 133. A method of claim 132, wherein the at least one other protein is synaptotagmin.

134. A method of claim 132, wherein the at least one other protein is laminin-1.

135. A method of claim 93, wherein the step of determining whether the compound or
30 agent modulates an activity of the SV2 protein comprises measuring transport of at least one substrate across a membrane.

136. A method of claim 135, wherein the at least one substrate is selected from the group consisting of amines, acetylcholine, excitatory neurotransmitters, GABA, serotonin, glycine or other amino acids, sugars and organic ions.

5

137. A method of claim 93, wherein the step of determining whether the compound or agent modulates an activity of the SV2 protein comprises measuring synaptic vesicle fusion, exocytosis, or synaptic vesicle recycling.

10

138. A method of identifying a binding partner for a SV2 protein, comprising:

- a) exposing a SV2 protein or fragment to a potential binding partner;
- b) incubating the protein or fragment and potential binding partner with (2S)-2-[4-(3-azidophenyl)-2-oxopyrrolidin-1-yl]butanamide; and
- c) determining if the binding of (2S)-2-[4-(3-azidophenyl)-2-oxopyrrolidin-1-yl]butanamide to the protein is inhibited by the potential binding partner, thereby identifying binding partner for the protein.

15

139. A method of identifying a compound or agent useful for the treatment of a neurological or endocrinological disorder, comprising:

20

- a) exposing a SV2 protein or fragment to the agent and levetiracetam or an analog or derivative thereof; and
- b) determining if the binding of levetiracetam or an analog or derivative thereof to the protein is modulated by the agent, thereby identifying an agent useful for the treatment of a neurological disorder.

25

140. A method of claim 139, wherein the analog of levetiracetam is (2S)-2-[4-(3-azidophenyl)-2-oxopyrrolidin-1-yl]butanamide.

141. A method of claim 139, wherein the SV2 protein or fragment is purified.

30

142. A method of claim 139, wherein the SV2 protein is human SV2A

143. A method of claim 142, wherein the SV2A protein comprises SEQ ID NO: 2.

144. A method of claim 139, wherein the SV2 protein or fragment is immobilized.

5

145. A method of claim 139, wherein the SV2 protein or fragment is expressed on a transformed host cell.

146. A method of claim 139, wherein the levetiracetam or an analog or derivative thereof is directly or indirectly labeled.

10

147. A method of claim 146, wherein the label is a radiolabel.

148. A method of claim 147, wherein the radiolabel is ³H.

15

149. A method of claim 146, wherein the label is a fluorescent label.

150. A method of claim 146, wherein the label is an enzyme.

151. A method of claim 139, wherein the SV2 protein or fragment is incubated with the levetiracetam or an analog or derivative prior to the agent.

20

152. A method of claim 139, wherein the SV2 protein or fragment is incubated with the levetiracetam or an analog or derivative after addition of the agent.

25

153. A method of claim 139, wherein the SV2 protein or fragment is incubated with the levetiracetam or an analog or derivative concurrent with the agent.

154. A method of claim 139, wherein the SV2 protein or fragment is incubated with levetiracetam.

30

155. A method of claim 139, wherein the neurological disorder is selected from the group consisting of epilepsy; epileptogenesis; seizure disorders; convulsions; withdrawal seizures; neurological disorders; bipolar disorders; mania; depression; anxiety; migraine; neuralgia; trigeminal neuralgia; chronic pain conditions; neuropathic pain; anaesthesia-related
5 hyperexcitability; cerebral ischemia; head trauma; myotonia; excitatory states provoked by drug or alcohol abuse, dependence or withdrawal; stroke; myoclonus; essential tremor; tics; Tourette's syndrome; dyskinesia; spasticity; movement disorders; neonatal cerebral haemorrhage; amyotrophic lateral sclerosis; Parkinson's disease; Alzheimer's disease; a neurodegenerative disease; and dementia.

10 156. A method of identifying an agent useful for the treatment of a neurological or endocrinological disorder, comprising:

- a) exposing a SV2 protein or fragment to the agent;
- b) incubating the protein or fragment and agent with (2S)-2-[4-(3-azidophenyl)-
15 2-oxopyrrolidin-1-yl]butanamide; and
- c) determining if the binding of (2S)-2-[4-(3-azidophenyl)-2-oxopyrrolidin-1-yl]butanamide to the protein is inhibited by the agent, thereby identifying binding partners for the protein.

20 157. A method of discovering or modeling an interaction between an SV2 protein, or fragment or derivative thereof, and a compound or agent selected from the group consisting of: levetiracetam, an analog or derivative of levetiracetam, or a compound or agent which competes with levetiracetam or an analog or derivative thereof for binding to the levetiracetam binding site comprising:

- 25 a) creating a 3-dimensional model of the SV2 protein, or fragments thereof, via either biochemical, biophysical, purely computational techniques, or some combination of these; and
- b) creating 3-dimensional model of one or a collection of potential ligands that might potentially bind the SV2 protein.

30 158. A method of claim 36 where the SV2 protein is purified from natural sources

159. A method of claim 36 where the SV2 protein is purified from heterologously expressed protein driven from a cloned nucleotide inserted in an expression vector, in a eukaryotic or prokaryotic host.

5 160. A method of claim 36 where the analysis is by proteolytic treatment of the SV2 proteins to observe a differential effect of binding of a ligand on proteolytic degradation.

161. A method of claim 40 where the SV2 protein is purified from natural sources

10 162. A method of claim 40 where the SV2 protein is purified from heterologously expressed protein driven from a cloned nucleotide inserted in an expression vector, in a eukaryotic or prokaryotic host.

15 163. A method of discovering or modeling an interaction between an SV2 protein and a compound or agent selected from the group consisting of: levetiracetam, an analog or derivative of levetiracetam, or a compound or agent which competes with levetiracetam or an analog or derivative thereof for binding to the levetiracetam binding site comprising:

20 a) determining a biochemical, pharmacological, organismal, cellular or molecular effect of a potential CNS active molecule in a genetically wild-type animal or in molecules, cells or tissues derived from such animals; and

b) comparing the measured effect of that compound in an equivalent study in a system with an SV2 protein knocked out or knocked down.

25 164. A pharmaceutical composition comprising a compound or agent as identified in the method of claim 139 said compound being different from a compound as described in Fig. 15.

30 165. A method of treating a neurological or endocrinological disorder which comprises administering to an individual in need of such treatment a compound or agent as identified in the method of claim 139 said compound being different from a compound as described in Fig. 15.

166. A method according to claim 165 wherein the neurological disorder is selected from the group consisting of epilepsy; epileptogenesis; seizure disorders; convulsions; withdrawal seizures; neurological disorders; bipolar disorders; mania; depression; anxiety; migraine; neuralgia; trigeminal neuralgia; chronic pain conditions; neuropathic pain; anaesthesia-related hyperexcitability; cerebral ischemia; head trauma; myotonia; excitatory states provoked by drug or alcohol abuse, dependence or withdrawal; stroke; myoclonus; essential tremor; tics; Tourette's syndrome; dyskinesia; spasticity; movement disorders; neonatal cerebral haemorrhage; amyotrophic lateral sclerosis; Parkinson's disease; Alzheimer's disease; a neurodegenerative disease; and dementia.

167. A method according to claim 165 wherein the endocrinological disorders is selected from the group consisting of endocrinopathies involving hypersecretion or hyposecretion of at least one hormone; gigantism; dwarfism; adrenal-medulla-related diseases; hypoglycemia; and circulation shock.

168. A pharmaceutical composition comprising a compound or agent as identified in the method of claim 93 said compound being different from a compound as described in Fig. 15.

169. A method of treating a neurological or endocrinological disorder which comprises administering to an individual in need of such treatment a compound or agent as identified in the method of claim 93 said compound being different from a compound as described in Fig. 15.

170. A method according to claim 169 wherein the neurological disorder associated with synaptic function is selected from the group consisting of epilepsy; epileptogenesis; seizure disorders; convulsions; withdrawal seizures; neurological disorders; bipolar disorders; mania; depression; anxiety; migraine; neuralgia; trigeminal neuralgia; chronic pain conditions; neuropathic pain; anaesthesia-related hyperexcitability; cerebral ischemia; head trauma; myotonia; excitatory states provoked by drug or alcohol abuse, dependence or withdrawal; stroke; myoclonus; essential tremor; tics; Tourette's syndrome; dyskinesia; spasticity; movement disorders; neonatal cerebral haemorrhage; amyotrophic lateral sclerosis;

Parkinson's disease; Alzheimer's disease; a neurodegenerative disease; and dementia.

171. A method according to claim 169 wherein the endocrinopathy or hormonal disease is selected from the group consisting of endocrinopathies involving hypersecretion or
5 hyposecretion of at least one hormone; gigantism; dwarfism; adrenal-medulla-related diseases; hypoglycemia; and circulation shock.

172. A method of claim 157, further comprising using purely computational techniques to
dock the 3-dimensional model of SV2 proteins with the 3-dimensional models of potential
10 ligands.